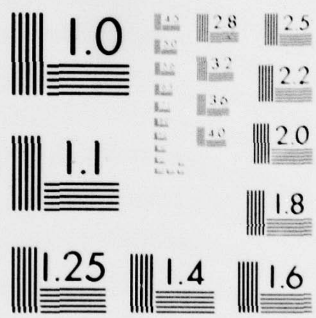
AD-A080 610 ARMY INST OF DENTAL RESEARCH WASHINGTON DC F/G 6/18
AN EVALUATION OF ACTINIC BLOCKING AGENTS,(U)
JAN 80 H P KESSLER, J G WEBB

UNCLASSIFIED NL

| OF |

AD
A080610

END
DATE
FILMED
3-80
DDC


1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0

LEVEL II

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER	2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle) AN EVALUATION OF ACTINIC BLOCKING AGENTS	5. TYPE OF REPORT & PERIOD COVERED Manuscript
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Harvey P. Kessler; Joseph G. Webb, Jr	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS U.S. Army Institute of Dental Research, Walter Reed Army Medical Center, Washington, DC 20012	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 12 15
11. CONTROLLING OFFICE NAME AND ADDRESS U.S. Army Medical Research & Development Com. HQDA (SGRD-RP) Washington, DC 20314	12. REPORT DATE 31 January 1980
	13. NUMBER OF PAGES 14
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)	15. SECURITY CLASS. (of this report) UNCLASSIFIED
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

This document has been approved for public release and sale; its distribution is unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

None

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Actinic radiation, ultraviolet light, actinic blockers

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Two actinic blocking agents, one for hot weather use and one for cold weather use, were tested for effectiveness and duration of protection. These materials are specifically designated for use as lip screens for the soldier during field operations. Each material proved inadequate in its ability to provide protection against damage by ultraviolet light. Statistically, both materials proved to be no better than no protection at all, even when tested immediately following its application. From this study it is not possible to determine whether the material is basically deficient as

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

038670 LB

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

20 (continued)

an actinic blocker or whether the shelf life of the active ingredient has been exceeded.

Accession For	
NTIS GRA&I	☑
DTIC TAB	☐
Unannounced	☐
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or special
A	

An Evaluation of Actinic Blocking Agents

MAJ Harvey P. Kessler, DC, USA*
LTC Joseph G. Webb, Jr., DC, USA**

Adverse environmental factors play an extremely important role in the effectiveness of the soldier in the field. One of the most common and recurring of these adverse environmental factors for the soldier is overexposure to actinic radiation. Such overexposure can result in acute or chronic damage to unprotected skin surfaces. The lips, because of their exposed position and their mucous membrane characteristics, are particularly susceptible to actinic damage. Because of this vulnerability, numerous agents have been developed to provide protection against harmful actinic radiation. The purpose of this study was to evaluate the effectiveness of actinic blocking agents issued to US Army personnel for lip protection during field operations.

LITERATURE REVIEW

Actinic radiation (sunlight) is composed primarily of visible, infrared, and ultraviolet light waves. It is the ultraviolet spectrum that produces harmful effects on the skin and lips.[11,12] Ultraviolet light is electromagnetic radiation with wavelengths of 220-400 nanometers (nm.). This can be further divided into ultraviolet light A,B, and C according to wavelength and properties.[11,12] Ultraviolet A is radiation with a wavelength of 320-400 nm. It has no detrimental effect on skin or mucous membrane but does act to augment the effects of any pigment already existing in the skin, allowing

---

From the US Army Institute of Dental Research, Walter Reed Army Medical Center, Washington, DC, 20012
*Presently staff pathologist, Dental and Oral Pathology, Armed Forces Institute of Pathology, Washington, DC, 20306
**Chief, Oral Pathology, DENTAC, Fort Ord, California, 93941

that pigment to function at maximum efficiency as a protective absorber. The effects of UV A are only temporary, fading within 24 hours and contributing little, if at all, to the formation of new pigment.[12] The effects of ultraviolet B (wavelengths of 280-320 nm.) range from a mild erythema to a red, painful sunburn with blistering occurring with increased exposure.[12] Forty-eight hours after exposure to UV B, there is increased production of melanin which rises into the stratum corneum. This increased production is an intricate process which involves several mechanisms: 1) an increase in the number of functional melanocytes by activation of dormant cells; 2) an increased arborization of melanocytic dendrites; 3) an increased number of melanosomes in melanocytes; 4) an increase in tyrosinase activity; and 5) an increase in transfer of melanosomes.[4] These responses all function to provide better protective absorption of UV light in the superficial skin layers.[4] Ultraviolet C is radiation with a wavelength of 220-280 nm. Its effects are the same as those of UV B, but occur more rapidly and tend to be more severe in the degree of damage produced.

On the earth's surface, ultraviolet light is received only in the wavelength range of 290-400 nm. The atmosphere, particularly the ozone layer, acts to absorb or scatter the most harmful, shorter wavelengths (UV C). With the sun directly overhead, the likelihood of tissue damage is maximal because the intensity of the radiation is greatest and absorption by the atmosphere is at the lowest level. When the sun is not directly overhead, the ultraviolet radiation assumes a longer, oblique path to the earth's surface, and, therefore, all atmospheric absorption processes are increased. This filters out the shorter ultraviolet B wavelengths and considerably reduces the intensity of all wavelengths.[11,12]

The harmful effects of ultraviolet radiation can be both acute and chronic. Acute damage (sunburn) is essentially no different than any other

burn-type injury in its pathogenesis. Damage caused by long term exposure to actinic radiation, however, is cumulative. It is manifested by histologic changes that include markedly increased ground substance, increased elastin formation, and decreased collagen formation in the connective tissue. This is also associated with atrophic epithelium with many abnormal cells in a disorderly pattern.[6,11,13] Damage is generally more severe in light-complected individuals.[5,11]

The lips present unique problems with respect to exposure to ultraviolet radiation. Normal skin has a thick keratin layer which protects against moderate exposure to UV light. Keratinization, however, is largely absent in the lips. The epithelium is thin and the dermal papillae are increased in number, penetrate deeper into the epithelium, and are more vascular than in the skin. There are no appendages present.[3] These factors enhance the possibility of UV injury.[4,13] The presence of a film of water or saliva on the surface has been shown to further enhance UV injury.[4,9,10] That the lip differs significantly from the skin has been demonstrated in a study by Payne[11] in which normally protective actinic blocking agents for skin use were shown to be less effective for use on the lips. The most effective agents for use on the skin were found, however, to be the most effective for use on the lips. Further complicating the situation is the difficulty of maintaining an actinic blocking agent on the lips because of the occasional wiping action of the tongue, especially those agents with an unusual feel.[11]

Actinic damage to the lips was once thought to be a problem associated only with older people. Knox et al.,[7] however, have reported moderate to severe actinic changes in one-third of persons 25-33 years of age. Kligman[6] observed moderate to severe damage in nearly 50% of subjects 20-29 years of age. Surprisingly, Kligman also noted moderate actinic damage in 20%

of subjects aged 10-19 years. The susceptibility of the soldier to actinic damage to the lips has been demonstrated in two separate studies. Bumstead and Laband[2] found a statistically significant correlation ($p < .01$) between lip lesions and outdoor duty in a survey of 996 Korean War Veterans 20-30 years of age. They also reported an increased incidence of malignant and premalignant lip lesions in their sample. Bernier and Clark,[1] in an extensive survey during World War II, also showed an increased incidence in lip lesions in those assigned to outdoor duty.

It is well documented that most of the acute and chronic damage resulting from overexposure to ultraviolet radiation is preventable.[11,12,15] Avoidance of overexposure to sunlight is the most obvious solution, but this goal is difficult, if not impossible, to achieve in military operations. The use of effective actinic blocking agents during military operations would, therefore, appear to be the most promising approach to control of this problem.

The ideal actinic blocking agent should provide a high degree of protection against sunburn anywhere on the earth's surface. It should maintain significant protection with normal usage. It should exhibit no photosensitization, contact sensitization, systemic or cutaneous toxic effects. The ideal blocking agent should also be acceptable cosmetically--colorless, odorless, non-greasy, pleasant, and easy to apply.[15]

Actinic blocking agents function by absorbing UV radiation, particularly in the ultraviolet B wavelengths of 300-307 nm., which are the most erythemogenic.[4,12] No currently available blocking agent is completely effective. The degree of protection varies greatly and is dependent on several factors. The active ingredient is of prime importance since it alone prevents the penetration of the UV radiation.[14] Other factors of importance include the vehicle,[8] the thickness of application of the agent and the ability of the material to withstand bathing, sweating, and abrasion.[12,14]

The vehicle is important because it functions to increase penetration of the active ingredient into the mucosa.[8] The thickness of application of the material is important because protection is not proportional to the thickness of the material but is related exponentially. Small differences in thickness of the application may exert significant effects on the absorption of the damaging radiation. The thicker the layer, the more protection provided.[12] The ability of the material to withstand sweating, bathing, and abrasion is also important, since the tongue may wet and wipe the lip surfaces. Materials which are easily removed by the actions of the tongue naturally provide less protection.[11,14,15]

METHODS AND MATERIALS

There are two lipscreening agents currently available for use by Army personnel in field operations; one is designated for hot weather use, the other for cold weather use. (Fig. 1) Each agent was tested for its effectiveness in preventing sunburn and for its duration of protection.

The ultraviolet light source was provided by a 950 Watt Xenon Solar Simulator.* This device employs a high intensity Xenon arc lamp which, with proper filtering, emits a spectrum of ultraviolet light almost identical to that received on the earth's surface. The beam of UV light is collimated through a metal disk with an exposure port of 4 mm. by 25 mm. The target-light distance, as well as the intensity of the light, remained fixed throughout the experiment.

The experimental animals utilized in the study were twelve white New Zealand rabbits, weighing 2-3 kg. In order to facilitate proper orientation of the animals to the Solar Simulator, each animal was anesthetized prior to exposure with 0.8-1.2 ml. (80-120 mg.) Vetalar (Ketamine Hydrochloride) and 0.5-0.75 ml. (10-15 mg.) Rompun. This dosage allowed ease of handling

*Solar Light Company, Philadelphia, Pa.

and proper orientation of the animals. Skin reaction to the actinic radiation was used as an indicator of UV exposure since there exists no suitable animal model for lip studies and the most effective actinic blocking agents for skin were also found to be the most effective for lip usage.[11]

Prior to evaluation of the actinic blocking agents, each rabbit was exposed to actinic radiation in order to determine its minimal erythema dose (MED). The MED is defined as the exposure time required to produce a clinically evident and sharply defined area of erythema at the exposure site when examined 24 hours after exposure. The MED was determined by a series of timed exposures. The rabbit was shaved just prior to determination of the MED to adequately expose the skin surface of the back. The exposed skin was then positioned against the exposure port and the Solar Simulator was activated for 10 seconds. Successive sites were exposed at 10 second intervals. The lowest exposure time that produced a sharply defined area of erythema 24 hours post-exposure was accepted as the MED. The MED for all rabbits was 50-60 seconds.

Following determination of the MED's, each rabbit was shaved in a previously unexposed area to expose the skin surface. Two coats of the actinic blocking agent for cold weather use was applied to the skin. A different tube of actinic blocking agent was used for each animal. The material was applied in a long narrow band parallel to the mid-sagittal plane. Each animal was then exposed for its MED. In all cases, the animal was oriented so that the exposure port was perpendicular to the mid-sagittal plane and overlapped unprotected skin surfaces on either side of the actinic blocking agent. This allowed each animal to act as its own control. To determine the duration of protection, the animals were exposed to the actinic radiation immediately after application of the actinic blocking agents and at intervals of 90 minutes

and 180 minutes post-application. Each exposure was performed at a separate site. Between exposures the animals were allowed normal activity in their cages but in no case was there further application of the lipscreening agents. The animals were examined for erythema at the test sites by each investigator 24 hours following the final exposure. Exposures were not scored unless an erythematous reaction was evident on each side of the "protected" area, where the exposure port overlapped unprotected skin. A positive erythematous reaction in areas where the blocking agent was applied was considered indicative of non-protection. (Fig. 2) Lack of erythema in the area of application of the blocking agent was considered indicative of protection. The procedure was then repeated for the actinic blocking agent designated for hot weather use, utilizing a previously unexposed area of the skin. The results for each material and each time interval were then evaluated for statistical significance utilizing the chi-squared statistical analysis.

In conducting the research the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as presented by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Research Council.

RESULTS

The agent designed for cold weather use, when exposed to actinic radiation immediately following its application, was protective in 3 cases and non-protective in 8 cases. The results on the twelfth animal were discarded due to a diffuse erythema produced by shaving too close to the skin surface. At 90 minutes post-application of the material, 10 animals showed no protection and one animal could not be evaluated since there was no evidence of erythema in the control areas immediately adjacent to the blocking agents. At 180 minutes, 10 animals showed no protection and again one animal could not be evaluated due to lack of erythema in the control area. The results are

summarized in Table I.

The agent designed for hot weather use was found to be protective in only one of twelve animals when exposed to actinic radiation immediately following its application. No protection was evident in any of the twelve animals at 90 minutes and eleven of the twelve showed no protection at 180 minutes. The twelfth animal could not be evaluated at the 180 minute interval due to lack of erythema at control sites. The results for hot weather material are summarized in Table II.

DISCUSSION

The materials tested in this study are standard U.S. Army supply items. They are intended for use by Army personnel during field operations, to be applied to the lips as a protective agent against the harmful effects of actinic radiation. These agents were obtained through normal supply channels and individual tubes were randomly selected for testing.

Twenty-seven percent of the samples designed for cold weather use were found to be protective against actinic radiation when tested immediately following application of the blocking agent. This protection was, however, not statistically significant when compared to unprotected skin (£ x^2=3.474, p =.05, df =1). The material was found to be completely non-protective in all cases at intervals of 90 minutes and 180 minutes following its application.

The hot weather material exhibited similar results. Only 8% of the tubes selected were found to be protective against actinic radiation immediately after its application. This was not significant when compared to unprotected skin (£ x^2=1.042, p =.05, df =1). This material was also found to be completely non-protective in all cases at intervals of 90 and 180 minutes after application.

This study indicates that, in rabbits, these actinic blocking agents, as presently supplied, are not protective against the harmful effects of actinic radiation. In this study, the actinic blocking agents were shown to be statistically no more dependable than using no protection at all.

These materials cannot be completely discounted as possible protective agents, however. It is possible that these materials might be protective when initially manufactured but lose their effectiveness due to degradation of the active ingredients with time. The time interval between manufacture and delivery to the soldier in the field has not been determined and perhaps exceeds the shelf life of the active ingredient (PABA). The materials need to be evaluated for their effectiveness as actinic blocking agents immediately following their manufacture. If they are found to provide adequate protection, then a better delivery system to the soldier must be implemented. If they are found to be non-protective, a better blocking agent needs to be provided.

SUMMARY AND CONCLUSIONS

Two actinic blocking agents, one for hot weather use and one for cold weather use, were tested for effectiveness and duration of protection. These materials are specifically designated for use as lip screens for the soldier during field operations. Each material proved inadequate in rabbits in its ability to provide protection against damage by ultraviolet light. Statistically, both materials proved to be no better than no protection at all, even when tested immediately following its application. From this study it is not possible to determine whether the material is basically deficient as an actinic blocker or whether the shelf life of the active ingredient has been exceeded.

REFERENCES

1. Bernier, J.L., and Clark, M.L.; "Squamous Cell Carcinoma of the Lip"; Milit. Med.; 109:370-405; 1951.

2. Bumstead, W.D., and Laband, P.F.; "Premalignant Lesions of the Lips in Soldiers Returning from Korea"; Oral Surg.; 8:64-75; 1955.

3. Cruickshank, B., Dodd, T.C., and Gardner, D.L.; Human Histology; The Williams and Wilkins Company, Baltimore, 1964; p. 53.

4. Fitzpatrick, T.B., and Haynes, H.A.; Principles of Internal Medicine, Edited by Harrison; McGraw-Hill; 7th Edition; 1974; pp. 281-282.

5. Gorlin, R.J., and Goldman, H.M., Editors; Thoma's Oral Pathology; C.V. Mosby Company, St. Louis; 6th Edition; 1970; pp. 826-829.

6. Kligman, A.M.; "Early Destructive Effect of Sunlight on Human Skin"; JAMA; 210:2377-2380; 1969.

7. Knox, J.M., Cockerell, E.G., and Freeman, R.G.; "Etiological Factors and Premature Aging"; JAMA; 179:630-638; 1962.

8. Kraft, E.R., et al; "The Importance of the Vehicle in Formulating Sunscreen and Tanning Preparations"; J. Soc. Cosmet. Chem.; 23:383-391; 1972.

9. Owens, D.W., et al; "Influence of Humidity on Ultraviolet Injury"; J. Invest. Dermatol.; 64:250-252; 1975.

10. Owens, D.W., et al: "Influence of Wind on Ultraviolet Injury"; Arch. Dermatol.; 109:200-201; 1974.

11. Payne, T.F.; "An Evaluation of Actinic Blocking Agents for the Protection of Lip Mucosa"; J. Am. Dent. Assoc.; 92:409-411; 1976.

12. Robertson, D.F.; "Solar Ultraviolet Radiation in Relation to Sunburn and Skin Cancer"; Med. J. Aust.; 2:1123-1132; 1968.

13. Sondergaard, J., and Greaves, M.W.; "Pharmacological Studies in Inflammation Due to Exposure to Ultraviolet Radiation"; J. Pathol.; 101:93; 1970.

14. The Medical Letter on Drugs and Therapeutics; "Sunscreens"; Vol. 16 No. 14, Issue 404; July 1974; p. 60.

15. Willis, I., and Kligman, A.M.; "Aminobenzoic Acid and Its Esters--The Quest for More Efficient Sunscreens"; Arch. Dermatol.; 102:405-417; 1970.

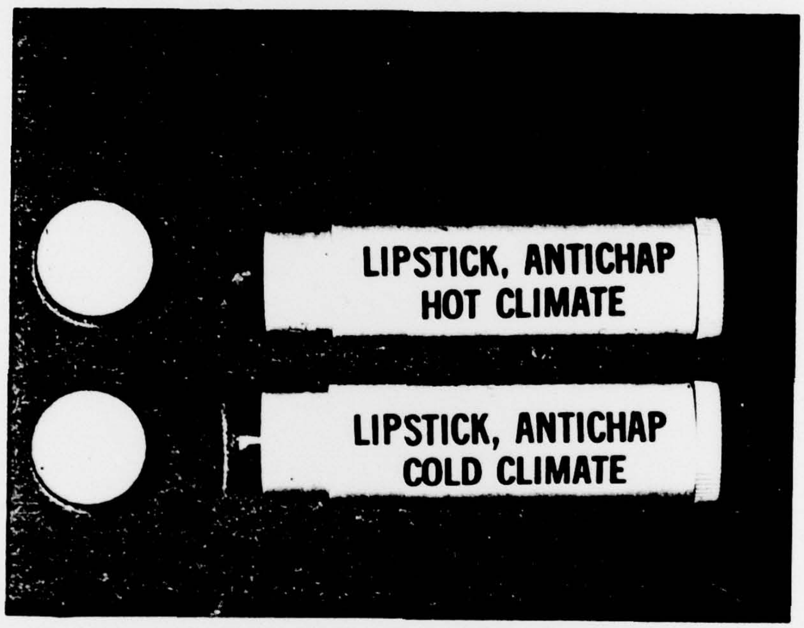


Fig. 1 The materials tested.

Fig. 2 Rabbit examined 24 hours post-exposure. Note the three erythematous zones overlapping the area of application of the blocking agent.

Table I

ACTINIC BLOCKING AGENT FOR COLD WEATHER USE

Animal #	Immed.	90 Min	180 Min
1. (261)	+	—	—
2. (259)	—	—	—
3. (254)	—	—	—
4. (751)	—	—	—
5. (79)	—	—	—
6. (173)	+	—	—
7. (998)	—	—	0
8. (77)	+	—	—
9. (78)	0*	0*	0*
10. (81)	—	—	—
11. (82)	—	0	—
12. (80)	—	—	—

+ = protection

— = non-protection

0 = no erythema on control

*Results discarded due to diffuse erythema probably caused by shaving animals too closely

Table II

ACTINIC BLOCKING AGENT FOR HOT WEATHER USE

Animal #	Immed.	90 Min	180 Min
1. (261)	—	—	0
2. (998)	—	—	—
3. (751)	—	—	—
4. (173)	—	—	—
5. (259)	—	—	—
6. (254)	—	—	—
7. (78)	—	—	—
8. (79)	—	—	—
9. (77)	—	—	—
10. (81)	+	—	—
11. (82)	—	—	—
12. (80)	—	—	—

+ = protection

— = non-protection

0 = no erythema on control